Claims:

1. An assay method for identifying a compound with ability to modulate interaction or binding between p21 and cyclin D1 and/or cdk 4, the method including:

(a) bringing into contact a substance which includes a peptide fragment of p21, or a derivative or analogue thereof, which is:

RERWNFDFVTETPLEGDFAW (peptide 4)

KACRRLFGPVDSEQLSRDCD (peptide 2)

KxxRRyFzP (wherein x may be any amino acid, y and z may be hydrophic, and each of the underlined residues may be absent or different)

KRRQTSMTDFYHSKRRLIFS (peptide 10)

KRRQTSATDFYHSKRRLIFS

TSMTDFYHSKRRLIFSKRKP (peptide 11)

KRRLIFSK, or

xyLzF (wherein y and z are any amino acid and x is preferably R),

a substance including cyclin D1 and/or cdk4, or a derivative or analogue thereof, and a test compound, under conditions wherein, in the absence of the test compound being an inhibitor of interaction or binding of said substances, said substances interact or bind; and

(b) determining interaction or binding between said substances.

2. An assay method according to claim 1 wherein the

fragment of p21, or derivative or analogue thereof, includes the amino acid sequence of peptide 4.

3. An assay method according to claim 1 wherein the fragment of p21, or derivative or analogue thereof, includes the amino acid sequence KxxRRyFzP.

4. An assay method according to claim 3 wherein the fragment of p21, or derivative or analogue thereof, includes the amino acid sequence of peptide 2.

5. An assay method according to claim 1 wherein the fragment of p21, or derivative or analogue thereof, includes the amino acid sequence xyLzF.

6. An assay method according to claim 5 wherein the fragment of p21, or derivative or analogue thereof, includes the amino acid sequence of peptide 10.

7. An assay method according to claim 5 wherein the fragment of p21, or derivative or analogue thereof, includes the amino acid sequence KRRLIFSK.

8. An assay method according to claim 7 wherein the fragment of p21, or derivative or analogue thereof, includes the amino acid sequence of peptide 11.

9. A method according to any one of claims 1 to 8

wherein a compound is additionally tested for ability to modulate a p21-mediated effect on cdk4 activity.

10. A method according to claim 9 wherein the cdk4 activity includes Rb phosphorylation.

11. A method according to claim 9 wherein induction of G1 cell-cycle arrest is tested.

12. A method which includes, following identification of a compound as being able to interfere with interaction or binding between p21 and cyclin D1 and/or cdk4 and/or modulate a p21-mediated effect on cdk4 activity in accordance with any of claims 1 to 11, formulation of the compound into a composition including at least one additional component.

13. Use of a substance which includes a peptide fragment of p21, or a derivative or analogue thereof, selected from:

RERWNFDFVTETPLEGDFAW (peptide 4)

KACRRLFGPVDSEQLSRDCD (peptide 2)

KxxRRyFzP (wherein x may be any amino acid, y and z may be hydrophic, and each of the underlined residues may be absent or different)

KRRQTSMTDFYHSKRRLIFS (peptide 10)

KRRQTSATDFYHSKRRLIFS

TSMTDFYHSKRRLIFSKRKP (peptide 11)

KRRLIFSK, or

xyLzF (wherein y and z are any amino acid and x is preferably R),

which is able to interact with or bind cyclin D1 and/or cdk4, in screening for compounds able to modulate interaction or binding between p21 and cyclin D1 and/or cdk4

14. Use of a substance which includes a peptide fragment of p21, or a derivative or analogue thereof, selected from:

RERWNFDFVTETPLEGDFAW (peptide 4)

KACRRLFGPVDSEQLSRDCD (peptide 2)

KxxRRyFzP (wherein x may be any amino acid, y and z may be hydrophic, and each of the underlined residues may be absent or different)

KRRQTSMTDFYHSKRRLIFS (peptide 10)

KRRQTSATDFYHSKRRLIFS

TSMTDFYHSKRRLIFSKRKP (peptide 11)

KRRLIFSK, or

xyLzF (wherein y and z are any amino acid and x is preferably R)

which is able to interact with or bind cyclin D1 and/or cdk4, in screening for compounds able to modulate a p21-mediated effect on cdk4 activity.

15. The use according to claim 14 wherein the cdk4 activity includes Rb phosphorylation.

16. The use according to claim 13 wherein induction of G1 cell-cycle arrest is tested.

17. The use according to any one of claims 13 to 16 wherein the p21 fragment, or derivative or analogue thereof, includes the amino acid sequence of peptide 4.

18. The use according to any one of claims 13 to 16 wherein the p21 fragment, or derivative or analogue thereof, includes the amino acid sequence KxxRRyFzP.

19. The use according to claim 18 wherein the p21 fragment, or derivative or analogue thereof, includes the amino acid sequence of peptide 2.

20. The use according to any of claims 13 to 16 wherein the p21 fragment, or derivative or analogue thereof includes the amino acid sequence xyLzF.

21. The use according to claim 26 wherein the p21 fragment, or derivative or analogue thereof includes the amino acid sequence of peptide 10.

22. The use according to claim 20 wherein the p21 fragment, or derivative or analogue thereof, includes the

amino acid sequence KRRLIFSK.

23. The use according to claim 23 wherein the p21 fragment, or derivative or analogue thereof, includes the amino acid sequence of peptide 11.

24. Use of a substance which comprises:

(i) a fragment of p21, or an active portion or derivative thereof;

(ii) a peptide fragment including the motif xyLzF, wherein y and z are any amino acid and x is preferably R, or a derivative of said peptide fragment with the property of inhibiting cdk4;

(iii) a peptide fragment including the motif KxxRRyFzP, wherein x is any amino acid, y and z may be hydrophic, and each of the underlined residues may be absent or different; or

(iii) a functional mimetic of (i), (ii) or (iii) with the property of inhibiting cdk4;

in the manufacture of a medicament for inhibiting cdk4, for the treatment of a disorder mediated by cdk4 activity, or for the treatment of a hyperproliferative disorder by inhibiting cdk4.

25. The use according to claim 24 wherein the substance comprises or consists essentially of a peptide fragment with a sequence which is:

Subq3

RERWNFDFVTETPLEGDFAW (peptide 4)

KACRRLFGPVDSEQLSRDCD (peptide 2)

KRRQTSMTDFYHSKRRLIFS (peptide 10)

KRRQTSATDFYHSKRRLIFS

TSMTDFYHSKRRLIFSKRKP (peptide 11)

or KRRLIFSK,

or a functional mimetic of any of these peptide sequences with the property of inhibiting cdk4.

26. The use according to claim 25 wherein the substance consists essentially of the peptide KRRLIFSK or a functional mimetic thereof with the property of inhibiting cdk4.

27. The use according to any one of claims 24 to 26 wherein the substance is coupled to a carrier for delivery to cells.

28. The use according to claim 27 wherein the substance is a peptide and is coupled to a carrier peptide with the sequence RQIKIWFQNRRMKWKK.

29. The peptide KRRLIFSK, or a functional mimetic thereof with the property of inhibiting cdk4, for use in a method of treatment of the human or animal body by therapy.

30. The peptide or functional mimetic thereof according

KACRRLFGPVDSEQLSRDCD (peptide 2)

KxxRRyFzP (wherein x may be any amino acid, y and z may be hydrophic, and each of the underlined residues may be absent or different)

KRRQTSMTDFYHSKRRLIFS (peptide 10)

KRRQTSATDFYHSKRRLIFS

TSMTDFYHSKRRLIFSKRKP (peptide 11)

KRRLIFSK, or

xyLzF (wherein y and z are any amino acid and x is preferably R)

or a derivative, fragment, analogue or functional mimetic of a said fragment.

33. A method according to claim 31 or claim 32 which takes place *in vitro* or *ex vivo*.

34. A method according to claim 31 or claim 32 which takes place *in vivo*.

35. Use of nucleic acid encoding a substance which comprises:

(i) a fragment of p21, or an active portion or derivative thereof;

(ii) a peptide fragment including the motif xyLzF, wherein y and z are any amino acid and x is preferably R, or a derivative of said peptide fragment with the property of inhibiting cdk4;

Subt 3

to claim 29 wherein the treatment is of a hyperproliferative disorder.

31. A method of interfering with interaction between p21 and cyclin D1 and/or cdk4, the method including contacting p21 and/or cdk4 with a substance which includes a peptide fragment of p21, or a derivative thereof, which is:

RERWNFDFVTETPLEGDFAW (peptide 4)

KACRRLFGPVDSEQLSRDCD (peptide 2)

KxxRRyFzP (wherein x may be any amino acid, y and z may be hydrophic, and each of the underlined residues may be absent or different)

KRRQTSMTAFYHSKRRLIFS (peptide 10)

KRRQTSATDFYHSKRRLIFS

TSMTDFYHSKRRLIFSKRKP (peptide 11)

KRRLIFSK, or

xyLzF (wherein y and z are any amino acid and x is preferably R),

or a derivative, fragment, analogue or functional mimetic of a said fragment.

32. A method of modulating a p21-mediated effect on cdk4 activity, the method including contacting p21 and/or cdk4 with a substance which includes a peptide fragment of p21, or a derivative thereof, which is:

RERWNFDFVTETPLEGDFAW (peptide 4)

(iii) a peptide fragment including the motif KxxRRyFzF, wherein x is any amino acid, y and z may be hydrophic, and each of the underlined residues may be absent or different; or

(iii) a functional mimetic of (i), (ii) or (iii) with the property of inhibiting cdk4;

in the manufacture of a medicament for inhibiting cdk4, for the treatment of a disorder mediated by cdk4 activity or for the treatment of a hyperproliferative disorder by inhibiting cdk4, by expression of the nucleic acid in a target cell.

36. The use according to claim 35 wherein the substance comprises or consists essentially of a peptide fragment with a sequence which is:

RERWNFDFVTETPLEGDFAW	(peptide 4)
KACRRLFGPVDSEQLSRDCD	(peptide 2)
KRRQTSMTDFYHSKRRLIFS	(peptide 10)
KRRQTSATDFYHSKRRLIFS	
TSMTDFYHSKRRLIFSKRKP	(peptide 11)
or KRRLIFSK	

or a functional mimetic of any of these peptide sequences with the property of inhibiting cdk4.

add A1 add B3 add B5

add B1 add C6